

The R¹ and R³ substituents of Holton and the R⁵ and R⁴ substituents of the present invention, respectively, are in comparison of varying scope. However, the -OR² substituent of Holton and the -O-C-O-R³R¹R² substituent of the present invention are directed toward hydroxyl protecting groups, as pointed out by the Examiner.

It is with respect to these groups that the Examiner directs his rejection. Specifically, the Examiner states, "It would be obvious to modify the lactam of Holton by replacing one hydroxy protecting group with another equivalent hydroxy protecting group as taught by Greene et al. to form the current lactam."

In order to establish a *prima facie* case of obviousness, there must be some teaching or suggestion to modify the teachings of the primary reference. Holton provides guidelines for selection of the hydroxyl protecting group. In the claims, Holton broadly defines R² as a hydroxyl protecting group. The definition of R² in the abstract, while only slightly less broad, specifically excludes the -O-C-O-R³R¹R² substituent of the present invention, and is limited to hydrogen, alkyl, acyl, acetal and ethoxyethyl. Holton further limits this broad category in the table at Column 12, lines 45-55. The preferred R² substituents are ethoxyethyl, SiR³, alkyl, ester, methoxymethyl, and 2,2,2-trichloroethoxymethyl.

In providing the above-preferred substituents for R², Holton also points out at Column 12, lines 36-39, "the hydroxyl protecting group selected should be easily removed under conditions that are sufficiently mild so as not to disturb the ester linkage or other substituents of the taxol intermediate." This statement emphasizes, as is well-known in the art, that all hydroxyl protecting groups are not equivalent. One following the teachings of Holton, would therefore, not be led to prepare the lactam of the present invention.

Furthermore, with respect to Greene et al., differences are pointed about between Holton's preferred ethoxyethyl ether and the 1-methyl-1methoxyethyl ether as claimed in the

present invention. At page 38, under the section relating to cleavage of ethoxyethyl ether, it states, "[ethoxyethyl] ether is more stable than the 1-methyl-1-methoxyethyl ether." One of skill in the art would not consider ethoxyethyl ether to be the equivalent of methyl methoxy ethyl ether, given these teachings. By pointing out this distinction, Greene teaches away from the use of methyl methoxy ethyl as an alternative for ethoxyethyl ether. *See Tec Air, Inc. v. Denso Mfg. Michigan, Inc.*, 52 USPQ2d 1294, 1298 (Fed. Cir. 1999), *citing In re Gurley*, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994) ("A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant or if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant.").

For the reasons set forth above, one following the teachings of Holton and Greene would not be led to prepare the lactam of the present invention. Therefore, reconsideration and withdrawal of the rejections under Section 103 are appropriate and respectfully requested.

Applicants submit the present claims are patentably distinct over the art and allowable in form. Early allowance is therefore solicited. The Examiner is encouraged to contact the undersigned attorney should there be any questions regarding this amendment.

Respectfully submitted,



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